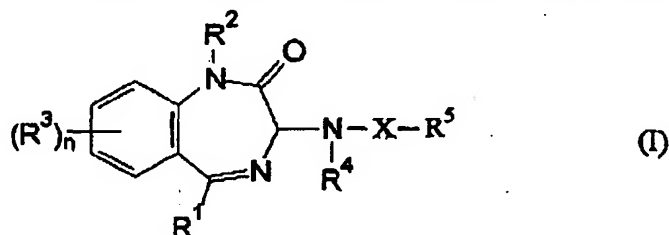


CLAIMS

1. Use of a compound which is (a) a benzodiazepine derivative of the formula
(I) or an N-oxide thereof or (b) a pharmaceutically acceptable salt thereof, in the
5 manufacture of a medicament for use in treating or preventing an RSV infection

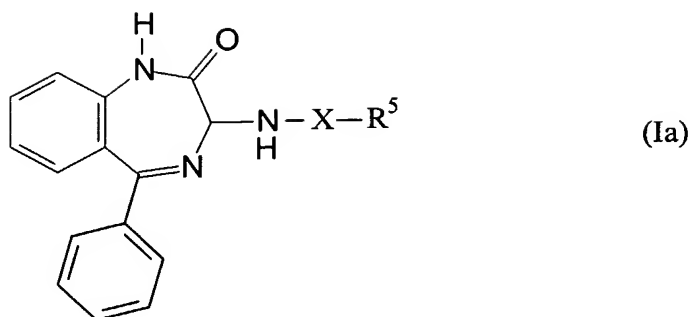


wherein:

- R¹ represents C₁₋₆ alkyl, aryl or heteroaryl;
- 10 - R² represents hydrogen or C₁₋₆ alkyl;
- each R³ is the same or different and represents halogen, hydroxy, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, amino, mono(C₁₋₆ alkyl)amino, di(C₁₋₆ alkyl)amino, nitro, cyano, -CO₂R', -CONR'R'', -NH-CO-R', -S(O)R', -S(O)₂R', -NH-S(O)₂R', -S(O)NR'R'' or -S(O)₂NR'R'', wherein each R' and
15 R'' is the same or different and represents hydrogen or C₁₋₆ alkyl;
- n is from 0 to 3;
- R⁴ represents hydrogen or C₁₋₆ alkyl;
- X represents -CO-, -CO-NR', -S(O)- or -S(O)₂-, wherein R' is hydrogen or a C₁-C₆ alkyl group; and
- 20 - R⁵ represents an aryl, heteroaryl or heterocyclyl group, which group is substituted by a C₁-C₆ hydroxyalkyl group or a -(C₁-C₄ alkyl)-X₁-(C₁-C₄ alkyl)-X₂-(C₁-C₄ alkyl) group, wherein X₁ represents -O-, -S- or -NR', wherein R' represents H or a C₁-C₄ alkyl group and X₂ represents -CO-, -SO- or -SO₂-, or R₅ represents -A₁-Y-A₂, wherein:
- 25 - A₁ is an aryl, heteroaryl, carbocyclyl or heterocyclyl group;
- Y represents a direct bond or a C₁-C₄ alkylene, -SO₂-, -CO-, -O-, -S- or -NR'-moiety, wherein R' is a C₁-C₆ alkyl group; and

- A₂ is an aryl, heteroaryl, carbocyclyl or heterocyclyl group.
- 2. Use according to claim 1, wherein R¹ is C₁₋₂ alkyl or phenyl.
- 5 3. Use according to claim 1 or 2, wherein R² is hydrogen.
- 4. Use according to any one of the preceding claims wherein R³ is halogen, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylthio, C₁₋₄ haloalkyl, C₁₋₄ haloalkoxy, amino, mono(C₁₋₄ alkyl)amino or di(C₁₋₄ alkyl)amino.
- 10 5. Use according to claim 4, wherein R³ is fluorine, chlorine, bromine, C₁₋₂ alkyl, C₁₋₂ alkoxy, C₁₋₂ alkylthio, C₁₋₂ haloalkyl, C₁₋₂ haloalkoxy, amino, mono(C₁₋₂ alkyl)amino or di (C₁₋₂ alkyl)amino.
- 15 6. Use according to any one of the preceding claims wherein R⁴ is hydrogen or C₁₋₂ alkyl.
- 7. Use according to any one of the preceding claims wherein X is -CO- or -CO-NR' - wherein R' represents hydrogen or a C₁₋₂ alkyl group.
- 20 8. Use according to any one of the preceding claims, wherein R⁵ is a 5- or 6-membered heterocyclyl or heteroaryl ring which is substituted by a C₁-C₆ hydroxyalkyl group or a -(C₁-C₄ alkyl)-X₁-(C₁-C₄ alkyl)-X₂-(C₁-C₄ alkyl) group, wherein X₁ and X₂ are as defined in claim 1.
- 25 9. Use according to claim 8, wherein R⁵ is a 5- or 6- membered heteroaryl group which is substituted by a -CH₂-OH or -(C₁-C₄ alkyl)-NR'-(C₁-C₄ alkyl)-S(O)₂-(C₁-C₄ alkyl) substituent, wherein R' is hydrogen or C₁-C₂ alkyl.
- 30 10. Use according to any one of the preceding claims, wherein A₁ is an aryl or heteroaryl group.

11. Use according to claim 10, wherein A₁ is a phenyl group, a monocyclic 5- or 6- membered heteroaryl group or a 5- to 6- membered heteroaryl group fused to a monocyclic oxo-substituted 5- to 6- membered heterocyclyl group.
- 5 12. Use according to any one of the preceding claims wherein A₁ is unsubstituted or substituted by 1 or 2 substituents selected from halogen, cyano, nitro, C₁-C₄ alkyl, C₁-C₄ haloalkyl and C₁-C₄ alkoxy substituents.
- 10 13. Use according to any one of the preceding claims, wherein Y represents a direct bond, a C₁-C₂ alkylene group, -SO₂- or -O-.
14. Use according to any one of the preceding claims, wherein A₂ is a phenyl, 5- to 6- membered heteroaryl, 5- to 6- membered heterocyclyl or C₃-C₆ cycloalkyl group.
- 15 15. Use according to any one of the preceding claims, wherein when A₂ is a heterocyclyl group it is attached to the moiety Y via a N atom.
16. Use according to any one of the preceding claims, wherein A₂ is unsubstituted or is substituted by 1 or 2 substituents which are selected from C₁-C₄ alkyl and halogen substituents when A₂ is a heteroaryl or aryl group and which are selected from C₁-C₄ alkyl, halogen and oxo substituents when A₂ is a carbocyclic or heterocyclyl group.
- 20 17. Use according to any one of the preceding claims, wherein A₂ is a piperazinyl, pyridyl, morpholinyl, pyrrolidinyl, piperidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group, which is unsubstituted or substituted by a C₁-C₂ alkyl group.
- 25 18. Use according to any one of the preceding claims wherein the benzodiazepine derivative of formula (I) is a benzodiazepine derivative of formula (Ia):
- 30



wherein:

- X is -CO- or -CO-NH- ; and
- 5 - R⁵ is a 5- to 6- membered heteroaryl group, for example a furanyl group, which is substituted by -CH₂-OH or -(C₁-C₄ alkyl)-N(CH₃)-(C₁-C₄ alkyl)-SO₂-(C₁-C₄ alkyl) or R₅ represents -A₁-Y-A₂, wherein:
 - A₁ is a phenyl, pyridyl, furanyl, thiazolyl, oxazolyl, isoxazolyl, thienyl or 1H-imidazo[4,5-b]pyridin-2-(3H)-one moiety, which is unsubstituted or substituted
 - 10 by 1 or 2 substituents selected from halogen, cyano, C₁-C₂ alkyl, C₁-C₂ haloalkyl and C₁-C₂ alkoxy substituents;
 - Y is a direct bond, a C₁-C₂ alkylene group, -SO₂- or -O-; and
 - A₂ is a piperazinyl, pyridyl, morpholinyl, pyrrolidinyl, piperidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group, which is unsubstituted or
 - 15 substituted by a C₁-C₂ alkyl group.

19. Use according to any one of the preceding claims, wherein the medicament is for use in treating a patient who is a child under two years of age, an adult suffering from asthma, chronic obstructive pulmonary disorder (COPD) or immunodeficiency,

20 an elderly person or a person in a long term care facility.

20. Use according to claim 19 wherein said child suffers from chronic lung disease.

25 21. Use according to any one of claims 1 to 18 wherein the medicament is for use in preventing RSV infection in an infant less than six years of age who was born after 32 weeks of gestation or less.

22. Use according to any one of the preceding claims, wherein the medicament is suitable for intranasal or intrabronchial administration.
- 5 23. Use according to any one of the preceding claims, wherein the medicament further comprises an anti-inflammatory compound or an anti-influenza compound.
24. Use according to claim 23 wherein the anti-inflammatory compound is budesonide or fluticasone.
- 10 25. Use according to claim 23 wherein the anti-inflammatory compound is a leukotriene antagonist, phosphodiesterase 4 inhibitor or TNF alpha inhibitor.
26. Use according to claim 23 wherein the anti-inflammatory compound is an
15 interleukin 8 or interleukin 9 inhibitor.
27. Use according to any one of claims 1 to 22 wherein the medicament is coadministered with an anti-inflammatory compound, as defined in any one of claims 24 to 26, or an anti-influenza compound.
- 20 28. A method of treating a patient suffering from or susceptible to an RSV infection, which method comprises administering to said patient an effective amount of a compound as defined in any one of claims 1 to 18.
- 25 29. A method according to claim 28, wherein said patient is a patient as defined in any one of claims 19 to 21.
30. A method according to claim 28 or 29, wherein said compound is administered intranasally or intrabronchially.
- 30 31. An inhaler or nebuliser containing a medicament which comprises
(a) a compound as defined in any one of claims 1 to 18, and

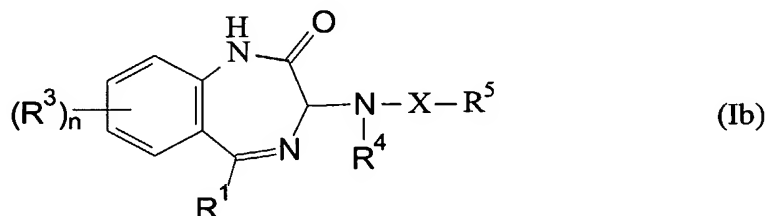
(b) a pharmaceutically acceptable carrier or diluent.

32. A product comprising a compound as defined in any one of claims 1 to 18
and an anti-inflammatory compound, as defined in any one of claims 24 to 26, or an
5 anti-influenza compound.

33. Use of a product according to claim 32 in the manufacture of a medicament
for use in the treatment of concomitant RSV and influenza infections.

10 34. Use of a compound as defined in any one of claims 1 to 18 in the
manufacture of a medicament for use in the treatment of human metapneumovirus,
measles, parainfluenza viruses, mumps, yellow fever virus (B5 strain), Dengue 2
virus or West Nile virus.

15 35. A compound which is (a) a benzodiazepine derivative of formula (Ib) or an
N-oxide thereof, or (b) a pharmaceutically acceptable salt thereof



20 wherein R_1 , R_3 , n , R_4 , X and R_5 are as defined in any one of claims 1 to 18.

36. A compound according to claim 35, wherein R_1 is an unsubstituted phenyl
group.

25 37. A compound according to claim 35 or 36, wherein when A_1 is a heteroaryl
group, it is other than a 5-methyl-isoxazolyl moiety.

38. A compound according to any one of claims 35 to 37, wherein A_1 is an aryl
or heteroaryl moiety.

39. A compound according to any one of claims 35 to 38, wherein X is -CO- or -CO-NR', wherein R' is as defined in any one of claims 1 to 18, provided that when X is -CO-NR', the moiety -A₁-Y-A₂ is -phenyl-O-phenyl.

5

40. A compound according to any one of claims 35 to 39, wherein A₂ is other than a 4- to 10- membered saturated cycloalkyl ring, in which one of the carbon atoms is replaced by a N atom.

10 41. A compound according to any one of claims 35 to 40, wherein A₂ is a piperazinyl, pyridyl, pyrrolidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group which is unsubstituted or is substituted by a C₁-C₂ alkyl group.

15 42. A compound according to claim 35, wherein the benzodiazepine derivative of the formula (Ib) is:

6-(4-Methyl-piperazin-1-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;

3,4,5,6-Tetrahydro-2H-[1,2']bipyridinyl-5'-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

20 (S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-Chloro-4-morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

25 (S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-4-fluoro-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-5-Chloro-2-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-5-fluoro-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

30 (S)-5-(4-Methyl-piperazin-1-ylmethyl)-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-5-Pyrrolidin-1-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-

- 1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-5-Piperidin-1-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-5-Dimethylaminomethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-
5 1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-4-Fluoro-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-piperidin-1-yl-benzamide;
(S)-4-Fluoro-2-morpholino-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
10 (S)-4-Cyano-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-yl-benzamide;
(S)-4-Cyano-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-piperidine-1-yl-benzamide;
(S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-
15 yl-4-trifluoromethyl-benzamide;
(S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-piperidin-1-yl-4-trifluoromethyl-benzamide;
(S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-4-trifluoromethyl-benzamide;
20 (S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-yl-5-trifluoromethyl-benzamide;
(S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-5-trifluoromethyl-benzamide;
(S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-
25 yl)-nicotinamide;
(S)-2-(1,1-Dioxo-1 λ 6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;
(S)-2-(1,1-Dioxo-1 λ 6-thiomorpholin-4-yl)-3-methyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
30 (S)-2-(1,1-Dioxo-1 λ 6-thiomorpholin-4-yl)-4-methyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-2-(1,1-Dioxo-1 λ 6-thiomorpholin-4-yl)-6-methyl-N-(2-oxo-5-phenyl-2,3-

- dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-2-Chloro-6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-3-Cyclopropyl-2-oxo-2,3-dihydro-imidazo[4,5-b]pyridine-1-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
5 (S)-3-(4-Methyl-piperazine-1-sulfonyl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-4-(4-Methyl-piperazin-1-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
10 (S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(piperidine-1-sulfonyl)-benzamide;
(S)-3-(Morpholine-4-sulfonyl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-5-Morpholin-4-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
15 (S)-5-Hydroxymethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-5-(1,1-Dioxo-1λ6-thiomorpholin-4-ylmethyl)-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
20 (S)-2-Chloro-4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-2-Chloro-5-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-5-([(2-Methanesulfonyl-ethyl)-methyl-amino]-methyl)-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
25 (S)-2-Pyridin-3-yl-thiazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-2-Pyridin-4-yl-thiazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
30 (S)-4-Methyl-2-pyrazin-2-yl-thiazole-5-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-2-Morpholin-4-ylmethyl-furan-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-

- 1H-benzo[e][1,4]diazepin-3-yl)-amide;
 (S)-3-Morpholin-4-ylmethyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
 (S)-5-Morpholin-4-ylmethyl-isoxazole-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
 (S)-3-Morpholin-4-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
 (S)-5-Pyridin-2-yl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
 (S)-2-Methyl-4-(morpholin-4-sulfonyl)-furan-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
 (S)-6-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;
 (S)-3-Morpholin-4-ylmethyl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
 (S)-5-Morpholin-4-ylmethyl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
 2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
 (S)-5-Phenyl-oxazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide; or
 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-phenoxyphenyl)-urea.
43. A compound according to any one of claims 35 to 42 for use in a method of treating the human or animal body.
44. A pharmaceutical composition comprising a compound according to any one of claims 35 to 43, and a pharmaceutically acceptable diluant or carrier.
45. A composition according to claim 44 comprising an optically active isomer of a compound according to any one of claims 35 to 42.

46. A composition according to claim 44 or 45 which is in the form of a tablet, troche, lozenge, aqueous or oily suspension, dispersible powders or granules.